Applicants
U.S. Scrial No.

: N. Rosen et al. : 09/445,054

Filing Date

: March 27, 2000

Page

: 2

40. (New) A method for achieving a synergistic therapeutic effect in a mammal in need thereof which comprises administering to said mammal amounts of at least two therapeutic agents selected from a group consisting of:

- a) a prenyl-protein transferase inhibitor and
- b) an antineoplastic agent which is a microtubule-stabilizing agent;

wherein the synergistic therapeutic effect is the treatment of cancers of the brain, breast, colon, genitourinary tract, lymphatic system, pancreas, rectum, stomach, larynx, liver, lung, prostate, stet histiocytic lymphoma lung adenocarcinoma, pancreatic carcinoma, colo-rectal carcinoma, small cell lung cancers and neurological tumor cancer whose growth is inhibited by the administration of the prenyl-protein transferase inhibitor and the antineoplastic agent.

- 41. (New) The method according to Claim 40 wherein an amount of a prenyl-protein transferase inhibitor and an amount of a microtubule-stabilizing agent are administered simultaneously.
- 42. (New) The method according to Claim 40 wherein an amount of a microtubule-stabilizing agent and an amount of a prenyl-protein transferase inhibitor are administered consecutively.
- 43. (New) The method according to Claim 40 wherein the antineoplastic agent is selected from: paclitaxel, epothilone A, epothilone B, desoxyepothilone A and desoxyepothilone B.
- 44. (New) The method according to Claim 40 wherein the prenyl-protein transferase inhibitor is selected from:
- 2(S)-Butyl-1-(2,3-diaminoprop-1-yl)-1-(1-naphthoyl)piperazine;
- I-(3-Amino-2-(2-naphthylmethylamino)prop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;

Applicants
U.S. Serial No.

: N. Rosen et al. : 09/445,054

Filing Date

: March 27, 2000

Page

- 2(S)-Butyl-1-{5-[1-(2-naphthylmethyl)]-4,5-dihydroimidazol}methyl-4-(1-naphthoyl)piperazine;
- 1-[5-(1-Benzylimidazol)mcthyl]-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-{5-{1-(4-nitrobenzyl)]imidazolylmethyl}-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-(3-Acetamidomethylthio-2(R)-aminoprop-1-yl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 2(S)-Butyl-1-[2-(1-imidazolyl)ethyl]sulfonyl-4-(1-naphthoyl)piperazine;
- 2(R)-Butyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)pipcrazine;
- 2(S)-Butyl-4-(1-naphthoyl)-1-(3-pyridylmethyl)piperazine;
- 1-2(S)-butyl-(2(R)-(4-nitrobenzyl)amino-3-hydroxypropyl)-4-(1-naphthoyl)piperazine;
- 1-(2(R)-Amino-3-hydroxyheptadecyl)-2(S)-butyl-4-(1-naphthoyl)-piperazine;
- 2(S)-Benzyl-1-imidazolyl-4-methyl-4-(1-naphthoyl)piperazine;
- 1-(2(R)-Amino-3-(3-benzylthio)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-(2(R)-Amino-3-[3-(4-nitrobenzylthio)propyl])-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 2(S)-Butyl-1-[(4-imidazolyl)ethyl]-4-(1-naphthoyl)piperazine;
- 2(S)-Butyl-1-[(4-imidazolyl)methyl]-4-(1-naphthoyl)pipcrazinc;
- 2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl)acetyl]-4-(1-naphthoyl)piperazine;

Applicants
U.S. Serial No.

N. Rosen et al.: 09/445.054

Filing Date

: March 27, 2000

Page

- 2(S)-Butyl-1-[(1-naphth-2-ylmethyl)-1H-imidazol-5-yl)ethyl]-4-(1-naphthoyl)piperazine;
- 1-(2(R)-Amino-3-hydroypropyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-(2(R)-Amino-4-hydroxybutyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-(2-Amino-3-(2-benzyloxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-(2-Amino-3-(2-hydroxyphenyl)propyl)-2(S)-butyl-4-(1-naphthoyl)piperazine;
- 1-[3-(4-imidazolyl)propyl]-2(S)-butyl-4-(1-naphthoyl)-piperazine;
- 2(S)-n-Butyl-4-(2,3-dimethylphenyl)-1-(4-imidazolylmethyl)-piperazin-5-one;
- 2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimethylphenyl)pipcrazin-5-one;
- 1-[1-(4-Cyanobenzyl)imidazol-5-ylmethyl]-4-(2,3-dimcthylphenyl)-2(S)-(2-methoxyethyl)piperazin-5-one;
- 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(1-naphthylmethyl)imidazol-5-ylmethyl]-piperazine;
- 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-naphthylmethyl)imidazol-5-ylmethyl]-piperazine;
- 2(S)-n-Butyl-1-[1-(4-cyanobenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;
- 2(S)-*n*-Butyl-1-[1-(4-methoxybenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;
- 2(S)-n-Butyl-1-[1-(3-methyl-2-butenyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;

: N. Rosen et al. **Applicants** U.S. Serial No. : 09/445.054 Filing Date : March 27, 2000 : 5

Page

- 2(S)-n-Butyl-1-[1-(4-fluorobenzyl)imidazol-5-ylmethyl]-4-(1naphthoyl)piperazine;
- 2(S)-n-Butyl-1-[1-(4-chlorobenzyl)imidazol-5-ylmethyl]-4-(1naphthoyl)piperazine;
- 1-[1-(4-Bromobenzyl)imidazol-5-ylmethyl]-2(S)-n-butyl-4-(1naphthoyl)piperazine;
- 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethylbenzyl)imidazol-5-ylmethyl]-piperazine;
- 2(S)-n-Butyl-1-[1-(4-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;
- 2(S)-n-Butyl-1-[1-(3-methylbenzyl)imidazol-5-ylmethyl]-4-(1-naphthoyl)piperazine;
- 1-[1-(4-Phenylbenzyl)imidazol-5-ylmcthyl]-2(S)-n-butyl-4-(1-naphthoyl)piperazine;
- 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(2-phenylethyl)imidazol-5-ylmethyl]piperazine;
- 2(S)-n-Butyl-4-(1-naphthoyl)-1-[1-(4-trifluoromethoxy)imidazol-5ylmethyl|piperazine;
- $1-\{[1-(4-cyanobcnzyl)-1H-imidazol-5-yl]acetyl\}-2(S)-n-butyl-4-(1-yanobcnzyl)-1H-imidazol-5-yl]acetyl\}$ naphthoyl)piperazine;
- (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(methanesulfonyl)ethyl]-2-piperazinone;
- (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)ethyl]-2-piperazinone;

Applicants : N. Rosen et al. U.S. Serial No. : 09/445,054 Filing Date : March 27, 2000

: 6

Page

- (R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethanesulfonyl)methyl]-2-piperazinone;
- (S)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[N-ethyl-2-acetamido]-2-piperazinone;
- (±)-5-(2-Butynyl)-1-(3-chlorophenyl)-4-[1-(4-cyanobenzyl)-5-inidazolylmethyl]-2-piperazinone;
- 1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;
- 5(S)-Butyl-4-[1-(4-cyanobenzyl-2-methyl)-5-imidazolylmethyl]-1-(2,3-dimethylphenyl)-piperazin-2-one;
- 4-[1-(2-(4-Cyanophenyl)-2-propyl)-5-imidazolylmethyl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)piperazin-2-one;
- 5(S)-n-Butyl-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-1-(2-methylphenyl)pipcrazin-2-one;
- 4-[1-(4-Cyanobenzyl)-5- imidazolylmethyl]-5(S)-(2-fluoroethyl)-1-(3-chlorophenyl)piperazin-2-one;
- 4-[3-(4-Cyanobenzyl)pyridin-4-yl]-1-(3-chlorophenyl)-5(S)-(2-methylsulfonylethyl)-piperazin-2-one;
- 4-[5-(4-Cyanobenzyl)-1-imidazolylethyl]-1-(3-chlorophenyl)piperazin-2-one;
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-homoserine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine lactone,

Applicants : N. Rosen et al. U.S. Serial No. : 09/445,054 Filing Date : March 27, 2000

Page: 7

- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-2-methyl-3-phenylpropionyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto)propylamino-3(S)-methyl]pentyloxy-4-pentenoyl-homoserine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-4-pentenoyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxypentanoyl-homoserine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylaniino-3(S)-methyl]pentyloxypentanoyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]5- pentyloxy-4-methylpentanoyl-homoserine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-4-methylpentanoyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercaptolpropylamino-3(S)-methyllpentyloxy-3-methylbutanoyl-homoserine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-methylbutanoyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylbutanoyl-homoserine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylbutanoyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine lactone,

TO: 703 308 4556

Applicants : N. Rosen et al. U.S. Serial No. : 09/445,054 Filing Date : March 27, 2000

Page

- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylthio-2-methyl-3-phenylpropionyl-homoserine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentylsulfonyl-2-methyl-3-phenylpropionyl-homoscrine lactone,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentylsulfonyl-2-methyl-3-phenylpropionyl-homoscrine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylaniino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine methyl ester,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine sulfone methyl ester,
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phenylpropionyl-methionine sulfone (Compound A),
- 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester,
- 2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-naphth-2-yl-propionyt-methionine sulfone methyl ester,
- 2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]-pentyloxy-3-naphth-2-yl-propionyl-methionine sulfone,
- 2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone methyl ester,
- 2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-naphth-1-yl-propionyl-methionine sulfone,

TO:703 308 4556

Applicants : N. Rosen et al. U.S. Serial No. : 09/445,054 Filing Date : March 27, 2000

: 9

Page

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyllpentyloxy-3-methybutanoyl-methionine methyl ester.

2-(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-methybutanoyl-methionine,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)methyl]pentyloxy-3-phenylpropionyl-homoserine lactone,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)-methyl]pentyloxy-3-phonylpropionyl-homoserine,

Disulphide of 2(S)-[2(S)-[2(R)-Amino-3-mercapto]propylamino-3(S)methyl]pentyloxy-3-methylbutanoyl-methionine methyl ester

1-(4-Biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Cyanobenzyl)-5-(4'-phenylbenzamido)ethyl-imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-Biphenylethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Bromo-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazolc

1-(2'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole 1-(4-(3',5'-dichloro)-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

Applicants U.S. Serial No.

: N. Rosen et al. : 09/445,054

Filing Date

: March 27, 2000

Page

: 10

1-(4-(3',5'-Bis-trifluoromethyl)-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)-4-methylimidazole

1-(4-Biphenylmethyl)-5-(4-cyanophenyloxy)-imidazole

5-(4-Cyanophenyloxy)-1-(2'-methyl-4-biphenylmethyl)-imidazole

5-(4-Biphenyloxy)-1-(4-cyanobenzyl)-imidazolc

5-(2'-Methyl-4-biphenoxy)-1-(4-cyanobenzyl)-imidazole

5-(4-(3',5'-dichloro)biphenylmethyl)-1-(4-cyanobenzyl)imidazolc

1-(4-biphenylmethyl)-5-(1-(R,S)-acetoxy-1-(4-cyanophenyl)methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-hydroxy-1-(4-cyanophenyl) methylimidazole

1-(4-Biphenylmethyl)-5-(1-(R,S)-amino-1-(4-cyanophenyl) methylimidazole

1-(4-biphenylmethyl)-5-(1-(R,S)-methoxy-1-(4-cyanophenyl)-methylimidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-oxo-1-(4-biphenyl)-methyl imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-fluoro-4-biphenyl)-methyl)- imidazole

1-(4-Cyanobenzyl)-5-(1-hydroxy-1-(3-biphenyl)mcthyl-imidazole

5-(2-[1,1'-Biphenyl]vinylene)-1-(4-cyanobenzyl)imidazole

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4-phenylbenzene

1-(4-Biphenylmethyl)-5-(4-bromophenyloxy)-imidazole

Applicants
U.S. Serial No.
Filing Date

: N. Rosen et al. : 09/445,054

Filing Date : March 27, 2000 Page : 11

1-(3'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Methyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(4'-Trifluoromethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Chloro-4-biphenylmethyl)-5-(4-cyanobcnzyl) imidazole

1-(4'-Chloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'3'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'4'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'5'-Dichloro-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(3'-Trifluoromethoxy-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazolc

1-(2'-Fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl) iniidazole

1-(4-(2'-Trifluoromethylphenyl)-2-Chlorophenylmcthyl)-5-(4-cyanobenzyl) imidazole

1-{1-(4-(2'-trifluoromethylphenyl)phenyl)ethyl}-5-(4-cyanobenzyl) imidazole

1-(2'-Trifluoromethyl-4-biphenylpropyl)-5-(4-cyanobenzyl) imidazole

1-(2'-N-t-Butoxycarbonylamino-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Acetylaminomethyl-4-biphenylmcthyl)-5-(4-cyanobenzyl) imidazole

Applicants U.S. Serial No.

: N. Rosen et al. : 09/445.054

Filing Date

: March 27, 2000

Page

: 12

1-(2'-Mcthylsulfonylaminomethyl-4-biphenylmcthyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Ethylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Phenylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazolc

1-(2'-Glycinylaminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmcthyl)-2-chloro-5-(4-cyanobenzyl) imidazole

1-(2'-Methyl-4-biphenylmethyl)- 4-chloro 5-(4-cyanobenzyl) imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl)imidazole

1-(3'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-4-(4-cyanobenzyl) imidazolc

1-(3'-Trifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3'-Methoxy-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Chloro-4'-fluoro-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-(2-Propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-(2-Methyl-2-propyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2'-Ethyl-4-biphenylmethyl)-5-(4-(1*H*-tetrazol-5-yl))benzyl)imidazole

1-[1-(4-Cyanobenzyl)imidazol-5-ylmethoxy]-4-(2'-methylphonyl)-2-(3-N-phthalimido-1-propyl)benzene

Applicants U.S. Scrial No. Filing Date

: N. Rosen et al. : 09/445,054

Page

: March 27, 2000

- 1-(3',5'-Ditrifluoromethyl-2-methyl-4-biphenylmethyl)-5-(4cyanobenzyl)imidazole
- 1-(3',5'-Chloro-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole
- 1-(3',5'-Dimethyl-2-methyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole
- 1-(3-(N-Boc-aminomethyl)-4-biphenylmethyl)-5-(4-cyanobenzyl)-imidazole
- 1-(3-Aminomethyl-4-biphenylmethyl)-5-(4-cyanobenzyl)imidazole
- 1-(4-Cyanobenzyl)-2-methyl-5-(2'-methylbiphenyl-4-yloxy)imidazole 5-(4-Cyanobenzyl)-1-(3-cyano-2'-trifluoromethylbiphenyl-4-ylmethyl)imidazole
- 2-Amino-5-(biphenyl-4-ylmethyl)-1-(4-cyanobenzyl)imidazole
- 2-Amino-1-(biphenyl-4-ylmethyl)-5-(4-cyanobenzyl)imidazole
- 1-(3-Butylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole
- 1-(3-Propylbiphenyl-4-ylmethyl)-5-(4-cyanobenzyl)-imidazole
- 1-(4-Biphenylmethyl)-4-(4-cyanobenzyl-2-methylimidazole
- 1-(4-Cyanobenzyl)-5-[(3-fluoro-4-biphenyl)methyl]imidazole
- 1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)-1-hydroxy]ethyl-2-methylimidazole
- 1-(4-Cyanobenzyl)-5-(4-biphenylmethyl)-2-methylimidazole
- 1-(4-Cyanobenzyl)-5-[1-(4-biphenyl)]ethyl-2-methyl imidazole
- 1-(4-Cyanobenzyl-5-[1-(4-biphenyl)]vinylidene-2-methylimidazole and
- 1-(4-Cyanobenzyl)-5-[2-(4-biphenyl)]vinylene-2-methylimidazole

Applicants
U.S. Serial No.
Filing Date

: N. Rosen et al. : 09/445,054

iling Date : March 27, 2000

Page : 14

1-(4-[Pyrid-2-yl]phenylmcthyl)-5-(4-cyanobenzyl)imidazole

1-(4-[3-Methylpyrazin-2-yl]phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(4-(Pyrimidinyl-5-yl)phenylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenylpyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Phenyl-N-Oxopyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-N-Oxopyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazolc

1-(2-(3-Trifluoromethoxyphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-(2-Trifluoromethylphenyl)-pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-2-Chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(3-Phenyl-4-chloropyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-Amino-3-phenylpyrid-6-ylmethyl)-5-(4-cyanobenzyl)imidazole

1-(2-[Pyrid-2-yl]pyrid-5-ylmethyl)-5-(4-cyanobenzyl)imidazole

N-{1-(4-Cyanobenzyl)-1H-imidazol-5-yl)methyl}-5-(pyrid-2-yl)-2-aminopyrimidine

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-4-[(3-carboxyphenyl)oxy]benzene

N,N-bis(4-Imidazolemethyl)amino-3-[(3-carbomethoxyphenyl)-oxy]benzene

N.N-bis(4-Imidazolemethyl)amino-4-[(3-carbomethoxyphenyl)-oxy]benzene

10.100 JOO JOSO

. N. Rosen et al.

Applicants U.S. Scrial No. Filing Date

: 09/445,054 : March 27, 2000

Page

: 15

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)aminomethyl-3-[(3carboxyphenyl)oxy]bcnzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)aminomethyl-3-[(3carbomethoxyphcnyl)oxy]benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-3-(phenoxy)benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-4-(phenoxy)benzene

N-(4-Imidazolemethyl)-N-(4-nitrobenzyl)amino-4-(phenylthio)benzene

N-Butyl-N-[1-(4-cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

N-[1-(4-Cyanobenzyl)-5-imidazolemethyl]amino-4-(phenoxy)benzene

N-(4-Imidazolemethyl)amino-3-[(3-carboxyphenyl)oxy]benzene

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzene

(±)-4-[(4-imidazolylmcthyl)amino]pentyl-1-(phenoxy)benzene

1-[(N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(n-butyl)amino)methyl]-4-(phenoxy)benzene

4-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylthio)benzene

(±)-4-[N-(1-(4-cyanobenzyl)-4-imidazolylmethyl)-N-(n-butyl)amino]-1-(phenylsulfinyl)benzene

3-[N-(4-imidazolylmethyl)-N-(n-butyl)amino]-N-(phenyl)benzenesulfonamide and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmethyl)amino]-3-methoxy-4phenylbenzene

Applicants : N. Rosen et al. U.S. Serial No. : 09/445,054

Filing Date : March 27, 2000
Page : 16

Page

: 16

4-{3-[4-(-2-Oxo-2-H-pyridin-1-yl)benzyl]-3-H-imidazol-4ylmcthyl]bcnzonitrile

4-{3-[4-3-Methyl-2-oxo-2-H-pyridin-1-yl)bcnzyl]-3-H-imidazol-4ylmethyl]benzonitrile

4-{3-[4-(-2-Oxo-piperidin-1-yl)benzyl]-3-H-imidazol-4-ylmethyl]benzonitrile

4-{3-[3-Methyl-4-(2-oxopiperidin-1-yl)-benzyl]-3-H-imidizol-4-ylmethyl}benzonitrile

(4-{3-[4-(2-Oxo-pyrrolidin-1-yl)-benzyl]-3H-imidizol-4-ylmethyl}-benzonitrile

4-{3-[4-(3-Methyl-2-oxo-2-H-pyrazin-1-yl)-benzyl-3-H-imidizol-4-ylmethyl}benzonitrile

4-{3-[2-Methoxy-4-(2-oxo-2-H-pyridin-1-yl)-benzyl]-3-H-imidizol-4ylmethyl}-benzonitrile

4-{1-[4-(5-Chloro-2-oxo-2H-pyridin-1-yl)-benzyl]-1H-pyrrol-2-ylmethyl}benzonitrile

4-[1-(2-Oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]benzonitrile

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]benzonitrile

4-[3-(2-Oxo-1-phenyl-1,2-dihydropyridin-4-ylmethyl)-3H-imidazol-4ylmethyl]benzonitrile

4-{3-[1-(3-Chloro-phenyl)-2-oxo-1,2-dihydropyridin-4-ylmethyl]-3H-imidazol-4-ylmethyl}benzonitrile

or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

nts

Applicants
U.S. Serial No.
Filing Date

: N. Rosen et al. : 09/445,054

Filing Date : March 27, 2000 Page : 17

45. (New) The method according to Claim 40 wherein the prenyl-protein transferase inhibitor is selected from:

2(S)-[2(S)-[2(R)-Amino-3-mercapto]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)

1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-2-piperazinone;

(R)-1-(3-Chlorophenyl)-4-[1-(4-cyanobenzyl)-5-imidazolylmethyl]-5-[2-(ethancsulfonyl)methyl]-2-piperazinone;

4-[1-(5-Chloro-2-oxo-2H-[1,2']bipyridinyl-5'-ylmethyl)-1H-pyrrol-2-ylmethyl]-benzonitrile and

1-[N-(1-(4-cyanobenzyl)-5-imidazolylmcthyl)-N-(4-cyanobenzyl)amino]-4-(phenoxy)benzenc

or a pharmaceutically acceptable salt, disulfide or optical isomer thereof.

46. (New) The method according to Claim 40 wherein the antineoplastic agent is paclitaxel and the prenyl-protein transferase inhibitor is 2(S)-[2(S)-[2(R)-Amino-3-mercapto]-propylamino-3(S)-methyl]-pentyloxy-3-phenylpropionyl-methionine sulfone isopropyl ester (Compound A)

Applicants
U.S. Serial No.
Filing Date
Page

: N. Rosen et al. : 09/445,054

: March 27, 2000

: 18

47.(New) A pharmaceutical composition comprising an amount of a prenyl-protein transferase inhibitor and an amount of an antineoplastic agent which is a microtubule-stabilizing agent, the composition which is effective for treating cancer in a mammal in need thereof.

48. (New) A method of preparing a pharmaceutical composition which comprises mixing an amount of a prenyl-protein transferase inhibitor and an amount of an antincoplastic agent which is a microtubule-stabilizing agent.